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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,799	07/19/2002	Jacinta Farn	20-02	3899

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,799	FARN ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-84* is/are pending in the application.

4a) Of the above claim(s) *39-62,67-71 and 73-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-66 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *39-84* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/6/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response to restriction requirement 11/4/03 is acknowledged. Claims 39-84 are pending in the application.

Election/Restriction

2. Applicant's election of Group I claims 63-66 and 72 drawn to polypeptide, SEQ ID NO: 5, 9/14/03 with traverse is acknowledged.

The traversal on the grounds that all the claims of the present application should be examined together because the claims of Groups I, II and III are indeed technically linked, i.e., the polypeptides of the Group I claims are encoded by the nucleic acid molecules of the Group II claims and the antibodies of Group III are directed to the polypeptides of the Group I claims. Because of this shared technical feature, it would not cause extra burden to the Patent Office to search and examine the invention simultaneously.

Applicants further point out that this request of simultaneous examination of all the claims herein is consistent with the restriction practice as governed by PCT practice as provided in the Administrative instructions under the PCT, Part 2, in Examples concerning "Unity of Invention" In particular, example 17.

Applicants further point out that claims 63-66 are directed to polypeptides which have an amino acid sequence as set out in SEQ .ID NO: 5. Claim 67 is directed to a polynucleotide that encodes a polypeptide having the sequence of SEQ ID NO: 5. Thus, claims 63-66 and 67 clearly share unity of invention. Similarly, the remainder of the claims of Group I directed to polypeptides share unity of invention with the claims of Group II directed to the corresponding polynucleotide sequence.

Applicants further submit that the claims of Groups I and III share common technical feature in that the claims directed to antibodies (Group III) define in part antibodies that

recognize the polypeptide sequence of SEQ ID NO: 5 and the antibodies are defined in the claims by reference to the polypeptide antigen, a conventional practice for defining antibodies. Thus, the claims directed to antibodies and polypeptides share unity of invention. Therefore, all the claims of the present application share unity of invention via common technical feature and should be examined together or at a minimum simultaneous examination of claims 63-66, 67, 72, 83 and 84 to the extent relevant to the sequence as set forth in SEQ ID NO: 5 should be examined.

The examiner disagrees with the applicant because although the applicant's above concept may link the Groups, such concept does not constitute a "special technical feature" as defined by PCT Rule 13.2 (37CFR1.475(a)). The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art." Specifically, Campos et al, U.S.Patent 6,096,320 teach this concept i.e., functional fragments of SEQ.ID.NO: 5, (see attached alignment of claimed SEQ.ID.NO: 5 with the haemotoxin of the prior art having several functional fragments such as LAQRVAAGLS), therefore it does not constitute" a special technical feature" by definition. Therefore, lack of unity is present and the examiner believes that the application has been filed under 35 U.S.C. 371, "Lack of Unity" practice is being followed.

Concerning arguments directed at the burden of search, it is noted that search burden is not criteria for unity of invention determination.

Therefore, claims 39-62, 67-71 and 73-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

Information Disclosure Statement

3. The Information Disclosure Statement filed on 9/06/02 has been reviewed and a signed copy of the same is attached to this application.

Specification - Informalities

4. Applicant should follow the direction or order or arrangement in framing the specification as provided in 37 CFR 1.77(b) since this is a utility application filed in USA. The specification should include all the sections in order. For example: Claims should begin with "I claim" or "'We claim" or "What is claimed is".

It is noted that Abstract of the Disclosure is missing. If applicant desires to include the abstract from PCT/AU00/ 01048, a copy of the abstract will be inserted in to the specification.

Claim Rejections - 35 USC 101

5. 35 U.S.C. 101 reads as Follows

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

6. Claims 63-66 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The product, a polypeptide as claimed, has the same characteristics as that found in nature. To overcome this rejection the Examiner suggests the amendment of the claims to include purity limitations, which would distinguish the characteristics of applicant's product from the product, as it exists in nature. It is further suggested that such limitation include the terminology " purified and isolated" (i.e. if such purity is supported in the specification) and/or a description of what applicant's protein is "free of" relative to the natural source. (see Farbenfabriken of Elberfeld Co. v. Kuehmsted, 171 Fed. 887, 890 (N.D. Ill. 1909) (text of claim at 889); Parke-Davis & Co. v. H.D. Mulford Co., 189 Fed. 95, 103, 106, 965 (S.D.N.Y. 1911) (claim 1); and In re Bergstrom, 427 F.2d 1394, 1398, 1401-1402 (CCPA 1970).

Claim Rejections - 35 USC 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 63-66 and 72 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

The claims are drawn to a polypeptide having an amino acid sequence, SEQ.ID.NO: 5 or a sequence having at least 60% or 70% or 90% identity with the sequence shown in SEQ.ID.NO: 5 or functional fragment thereof, having haemolysin activity. Claims are also drawn to a composition comprising said polypeptide and optionally a carrier and/or adjuvant.

The specification broadly describes as part of the invention, an isolated recombinant polypeptide comprising an amino acid sequence, SEQ ID NO: 5, which is encoded by Moraxella bovis strain Dalton 2d. The specification also teaches on page 25 that this full-length protein contains 927 amino acids with a molecular weight 98.8 kD. At the amino acid level it appears that this haemolysin gene product shows similarities with a subunit of the RTX and other haemolysins. However, the specification does not teach a sequence having at least 60% or 70% or 90% identity with the sequence shown in SEQ.ID.NO: 5 or functional fragment thereof.

The actual biological function of the protein represented as SEQ ID NO: 5 is not set forth in this specification. Applicants broadly describe the invention as embracing any deletion by use of language in which a specified percent of amino acids can be changed in the protein. USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, an isolated polypeptide comprising the amino acid, SEQ ID NO: 5 and composition comprising said polypeptide meets the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below.

The specification fails to teach polypeptide fragments of SEQ ID NO: 5 and it is noted that the claimed fragments do not exist as an invention independent of their function in encoding a protein, SEQ.ID.NO: 5. The actual structure or other relevant identifying characteristics of each protein fragment having the claimed properties of the protein can only be determined empirically by actually making every nucleic acid that encodes the recited fragments and testing each to determine whether such a fragment has the particularly disclosed properties of full length protein. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function. This specification does not teach functional fragments of SEQ.ID.NO: 5. There is no written description support for an isolated a sequence having at least 60% or 70% or 90% identity with the sequence shown in SEQ.ID.NO: 5 or functional fragment thereof as claimed.

The isolated polypeptide comprising SEQ ID NO: 5 is uncharacterized by this specification and is asserted to belong to haemolysin family of proteins. The specification fails to teach the structure or relevant identifying characteristics of a representative number of SEQ.ID.NO: 5 fragments, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

9. Claims 63-66 and 72 are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide or a composition comprising the amino acid sequence SEQ ID NO: 5 does not reasonably provide enablement for a polypeptide having at least 60% or 70% or 90% identity with the sequence shown in SEQ.ID.NO: 5 or functional fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are discussed supra

The nature of the invention is preparation of recombinant polypeptides and its use a vaccine preparation against *Moraxella bovis* infection. The specification teaches the production of recombinant polypeptide comprising the amino acid sequence, SEQ ID NO: 5, which is encoded by *Moraxella bovis* strain Dalton 2d. The specification also teaches on page 25 that this full-length protein contains 928 amino acids with a molecular weight 98.8 kD. At the amino acid level it appears that this haemolysin gene product shows similarities with a subunit of the

RTX and other haemolysins. However, the specification fails to teach polypeptide having at least 60% or 70% or 90% identity with the sequence shown in SEQ.ID.NO: 5 or functional fragment thereof. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid sequences (i.e. fragments) for different aspects of biological activity cannot be predicted a priori and must be determined empirically on a case-by-case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis in proteins. Such proteins differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Applicants have not taught which residues of SEQ ID NO: 5 can be varied and still achieve a polypeptide that is

functional as a vaccine or is capable of use as a diagnostic using immunological means of recognition. Since, the specification lacks a written description of any fragment of SEQ ID NO: 5, it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed chemical structure of the claimed polypeptide fragments of SEQ ID NO: 5. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

Claim Rejections - 35 USC 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 63-66 and 72 are rejected under 35 U.S.C. 102(e) as being anticipated by Campos et al U.S.Patent: 6,096,320

The claims are drawn to a polypeptide having an amino acid sequence, SEQ.ID.NO: 5 or a sequence having at least 60%, 70% or 90% identity with the sequence shown in SEQ.ID.NO: 5 or functional fragment thereof, having haemolysin activity. Claims are also drawn to a composition comprising said polypeptide and optionally a carrier and/or adjuvant. The examiner

is viewing the claims 64 and 65 as a sequence having at least 70% or 90% identity to a sequence having 60% identity as recited in claim 63.

Campos et al 1994 disclose a recombinant P. hemolytic leukotoxin polypeptide fused to IL2 (IL2-LKT, see Example 1) and thus read on the claims which broadly recite a sequence having at least 70% or 90% identity to a sequence having 60% identity including functional fragments as the disclosed polypeptide contains a sequence having less than 60% identity. This polypeptide contains several functional fragments (see alignment of SEQ ID NO: 2 of the prior art with the disclosed SEQ.ID.NO: 5) such as LAQRVAAGLS, having haemolysin activity (see column 16, lines 40-56) and read on . The prior art also discloses a composition comprising recombinant P. haemolytica leukotoxin in phosphate buffered saline (i.e., carrier) with Emulsigen as the adjuvant (see column 19, lines 1-11). Thus the prior art anticipated the claimed invention.

12. Claims 63-66 and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Billson, F. M. et a1. (1994) FEMS Microbiology 124:69-73.

The claims are discussed supra.

Billson et al disclose a vaccine composition comprising the haemolytic strain M. bovis isolate UQV 148NF containing haemolysin antigen, formaldehyde (carrier) was added to concentrated cell-free preparation and each preparation formulated in incomplete Freund's adjuvant (see page 70, left column, under preparation of vaccine antigen through right column).

Applicant's use of the open-ended term "comprising " in the composition claim fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Therefore, the claims read on the disclosed haemolytic vaccine antigens which inherently comprises the amino acid sequence as set forth in the SEQ.ID.NO: 5 or functional fragments. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79

(C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the disclosed prior art protein and the claimed polypeptide are the same since polypeptides are neither purified nor isolated. Since the Office does not have the facilities for examining and comparing applicants' claimed polypeptide and composition having said polypeptide with the prior art haemolysin antigen the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

14 No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (571) 272-0853. The examiner can normally be reached on Monday through Friday from 6:30 A.M. to 4:00 P.M. EST, First Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600

Padma Baskar Ph.D.

2/18/04

PATRICIA A. DUFFY
PRIMARY EXAMINER